ART. III.—*Remarks on the Etiology of Choked Disk in Brain Disease.*

By EDWARD G. LORING, M.D., of New York. (With a wood-cut.)

FEW more interesting problems have ever been offered to the student of medicine in its broadest and most comprehensive sense than that embraced in the connection between the eye and the brain and the ability to determine with the ophthalmoscope the morbid conditions of the one from those of the other.

This is particularly true in regard to optic neuritis, and chiefly in respect of the special form known as "Stauungspapille" or choked disk, the true cause of which has excited and is still exciting so much discussion.

The great difficulty, as well as interest, of the problem is shown quite as much by the eager haste with which the majority have accepted the theories successively offered to them, as by the ingenuity and plausibility of the arguments advanced in support of these theories.

The three most prominent theories brought forward to account for the production of choked disk have been in turn that of Graefe, that of Benedikt, and that of Schmidt. This last was founded upon the physiological researches of Schwalbe, and perhaps because it is the last, and perhaps too a little out of desperation, it has been accepted almost universally, both at home and abroad, as the true explanation of the group of appearances seen in Stauungspapille.

It is to the last of the three that the following remarks will mostly apply, only enough being said in regard to the former two to render a discussion of the last possible.

In a paper read before the Society of Neurology and Electrology, it was shown from the anatomical structure of the eye, from numerous physiological experiments, and post-mortem examinations, that there was every reason for believing that the circulation of the eye, though derived directly from that of the brain, was to a marked degree independent of it. That is to say, that the eye itself through the intraocular pressure possessed a self-regulating power, so that the circulation in the cranium might be seriously interfered with, by ligation of the vessels in the neck, and by other means, and yet that of the eye remain unaffected.

Notwithstanding this apparent want of sympathy between the circulation of the eye and brain, Graefe, nearly twenty years ago, announced the belief that the circulation of the eye might, so to speak, be looked upon as the visible index of the condition of the intra-cranial pressure, so that any increase in this would show itself by a change in the condition of the vessels of the disk, which would be expressed, if sufficiently marked, in the complex of appearances known as "choked disk."

In considering this theory of Graefe, it is important, at the outset, to bear in mind that the term intra-cranial pressure has no reference to the relative quantities of blood or other fluid at a given moment in the brain, or even to the condition of the cerebral substance, but is simply used in reference to and in comparison with the normal equilibrium which exists between the lateral pressure of the united contents of the cranial cavity, and its resisting walls.

The essential point, therefore, in Graefe's theory was the disturbance of the normal amount by an increase in the lateral pressure, which would show itself at the optic nerve entrance. The manner in which this increase in pressure was brought to bear on the somewhat distant circulation of the eye was, according to Graefe, purely mechanical, and is briefly as follows:—

If the intra-cranial pressure be increased, this will be reflected in all directions, and of course exert its influence upon the cavernous sinus. As the vein is more compressible than the artery, it will be the first to yield to the pressure. An impediment to the return circulation through the ophthalmic and retinal vein would take place, and there would be a banking up, so to speak, of the venous current, especially when it met the constriction, or collar, formed by the sclera round the ocular end of the nerve as it pierces the globe. Here, on account of this anatomical constriction, swelling from irritation of the surrounding parts would occur. This would only increase the trouble till almost complete strangulation took place, followed by all the peculiar ophthalmoscopic signs, and morbid appearances, shown in microscopic sections.

The peculiar symptoms of Stauungspapille might, according to Graefe, spring from any cause which increased intra-cranial pressure, such as tumour, meningitis, dropsy of the ventricle, hypersecretion of the subarachnoidal or cerebro-spinal fluid. Nor did the size or position of the tumour or growth have any significance. It might be the size of a cherry or as large as an orange; and it might occupy any position, provided irritation enough was created to produce an increased pressure of the contents of the cranium. Here, too, it should be borne in mind that all cases of disease, whether of the brain or investing membranes, are not necessarily followed by increased intra-cranial pressure. On the contrary there is no reason why the originally normal tissue should not be supplanted in the cavity of the head, as it is so often in the eye, by an abnormal growth which so gradually takes the place of the pre-existing tissue as to cause no disturbance to the normal equilibrium of pressure. That this may happen in the case of large growths, experience proves; while on the other hand the smallest growth for some unaccountable reason may excite so much irritation to the surrounding parts, or in some subtle way so affect the vessels themselves, as to produce increased pressure, either through excess of the fluid or expansion of the solid contents of the cranium.

That there should be intermissions and remissions of these attacks of inflammatory irritation, when the disease itself and its influence on the surrounding parts should remain quiescent, is as natural here as in other parts of the body.

Graefe's theory was considered sufficient for some years, supported as it was both by clinical observation and post-mortem examinations. Objections to it gradually began to be heard, however, and these took a definite shape in a paper written by Benedikt in 1868.[1] He asserted: First, that the growth was often too insignificant and of too mild and non-inflammatory a nature to set up such a degree of pressure in the head as to affect so distant a circulation as that of the eye. Secondly, that clinical experience taught that the neuro-retinitis might abate entirely without any reduction of the tumour. Thirdly, it was hard to see why pressure should offer hinderance to no other circulation, and should set up morbid action in no other nerve district than that of the eye.

Benedikt's views in opposition to the pressure theory and those in support of his own are too numerous and too long to receive further discussion here, though much might be said, as indeed it has been, in opposition to his arguments against Graefe's views, while much that he offers in favour of his own theory is untenable.[2] The theory itself was, that some irritation was brought to bear on the sympathetic nerves, and that this irritation was propagated in some subtle way to the vasa-motor filaments which regulated the circulation of the disk;—in other words, that the neuritis was one of abnormal innervation of the sympathetic system.

This theory of Benedikt's is certainly a very plausible one, and there is much in its favour which has never been satisfactorily refuted, though this in itself may be due to its vague and intangible nature, which seems to defy anything like actual demonstration.

Following the theoretical objections of Benedikt came the anatomical ones of Sesemann.[3] His objections to the pressure theory are important, and are as follows:—

1. "The cavernous sinus is a blood canal surrounded by such impervious walls as are rarely met with, and a pressure sufficient to really compress this must, since the pressure within the cranium must be regarded as equal in all directions, exercise enormous pressure on all the other bloodvessels.
2. "Both the superior and inferior ophthalmic vein anastomose extensively with one another, and also with the facial vein, and although the vena centralis retinæ empties itself almost immediately into the cavernous sinus, yet it previously anastomoses with the superior ophthalmic vein. So long then as the facial vein is open, the blood from the central vein of the retina could pass unimpeded through it.
3. "All increase of cerebral pressure is not followed by neuritis.
4. "Optic neuritis is sometimes one-sided, and has been observed on the side opposite the eye affected."

Forcible as these objections are, they are not, however, it seems to me, conclusive. In the first place, it has never been proved that increased pressure must necessarily be extended equally in all directions, as it no doubt would be were the cranium a simple sphere. It must, however, be borne in mind that the brain is divided by numerous partitions, in the shape of fibrous and inelastic membranes, which are at numerous places bound down firmly to bony attachments, so that it is easily conceivable that pressure sufficient to exert an influence on some delicate nerve fibres might exist in one part of the brain and yet not extend itself to all others, or, the pressure existing in one portion of the brain, its effects might be propagated to a more distant portion through the medium of the nerves, especially the vaso-motor filaments.

---

[1] Elecktrotherapie, Wien, 1868, p. 249.

[2] Archiv Anat. Phys., etc., pt. 2, p. 154, 1869.

[3] For a discussion of this subject see Allbutt, *On the Ophthalmoscope.*

The fact that neuritis optica occurring on one side only could not exist under the pressure theory, is based on the assumption that the pressure is always equally distributed in all directions.

Another forcible argument against Graefe's theory might be brought forward in the fact that we may have the return circulation through the ophthalmic vein interfered with, caused, as shown on the autopsy, by some obstruction in the orbit or in the vein itself, and yet no impediment to the circulation through the retinal vein occur. Cases, though rare, are yet occasionally met with, where exophthalmos of a large amount exists on one side, and where marked interference to the return circulation through the ophthalmic vein is undoubtedly present, with a large degree of distension and tortuosity of the supra-orbital and other superficial branches of the facial, and yet where the ophthalmoscope shows that the fundus of the eye is perfectly normal, and where there is not a particle of interference in the circulation of the central retinal vein. This could not be if the theory of choked disk was based on a mere mechanical impediment to the return blood into the sinus by way of the ophthalmic vein.

The fact that in these cases, the retinal circulation was undisturbed would go to support Sesemann's view, that, if the passage through the ophthalmic to the sinus was blocked, the blood from the central vein of the retina could pass unimpeded by the facial vein by means of the anastomosis which exists between this and the ophthalmic vein.

About the same time that these objections were brought forward by Sesemann, Schwalbe[1] was making his investigations into the lymph spaces of the eye and optic nerve. He found, that, by injecting fluid under the arachnoidal membrane of man as well as of the lower animals, that is to say, into the subarachnoidal space, the fluid forced itself under a moderate pressure into the space between the outer and inner sheath of the optic nerve.

These experiments by Schwalbe were followed by others of the same character by Schmidt,[2] Wolfring,[3] and Michel,[4] and others. And although there were discrepancies of greater or less significance in the results obtained by the various observers, all agreed upon the one important point which interests us here, and that is, that fluid would pass from the subarachnoidal space in the brain into the space formed by the two sheaths of the optic nerve. It was claimed, therefore, that the fluid when it arrived at the ocular end of the optic nerve, would occasion stasis of the circulation and all the phenomena expressed in neuritis or choked disk; and it is claimed also that this must be the true explanation, because fluid has actually been found between the two sheaths in some of these cases which have come to autopsy.

---

[1] M. Schultze's Archiv, Bd. vi., 1869.

[2] Archiv, Bd. xv. 2, 1869.

[3] Archiv für Ophth., Bd. 18, 2, 1872.

[4] Archiv für Ophth., Bd. 18, 1, 1872.

But it by no means follows, it appears to me, that, because fluid has been found in some cases of neuritis between the sheaths of the nerve, this necessarily has come down from the brain.

There are certain anatomical considerations which would render such a passage of the fluid very difficult. For, admitting that the fluid was in such quantities within the cranium as to fill the spino-arachnoidal space and the base of the skull, and admitting, too, that the pressure was sufficient to force the fluid between the sheaths, there are still other anatomical factors which would play an important part, both as cause and effect. For it must be remembered that the optic foramen is a bony canal of only a moderate diameter, and that the optic nerve and investing membrane fit it pretty exactly. Moreover, through this bony canal passes the ophthalmic artery.

If fluid was forced between the sheaths in this bony canal, it would cause the same irritation at this end of the nerve that it is claimed it does when it has arrived at the bulbar end. There would be swelling of the parts, with compression, especially as they are inclosed within bony walls. Either the nerve would be compressed and vision would suffer, or the ophthalmic artery would be compressed, and the circulation of the orbit would be interfered with. Now, it often happens that vision in the most pronounced cases of Stauungspapille is not disturbed,[1] nor is there the slightest interference with the circulation of the orbit.

Again, if fluid was forced by these resisting parts, irritation would be set up, and we should have inflammation not only of the investing membranes, but also of the trunk of the nerve, and it usually happens in choked disk that the end of the nerve is perfectly free from disease, while the end near the eye is affected.

Moreover, if swelling of the cranial end of the nerve and the surrounding parts did take place, then not only the two sheaths of the optic nerve would be pressed together, cutting off their connection with the corresponding spaces in the head, but the inner sheath would also be pressed against the trunk, and the lymphatics[1] proved to exist beneath this sheath would also have their connections severed, and their contents, instead of being carried into the cranial cavity, would be backed up in the nerve, and especially between the sheaths. The expression of this stasis would then be not so much at the cranial end of the nerve as at the ocular, for at the cranial end the sheaths are in more intimate relation with the trunk of the nerve, and the nerve is more closely embraced by the tendons of the various muscles and orbital tissues. It would, on the contrary, have a freer expansion near the bulb, and this is just where we find the distension of the sheath the greatest.

---

[1] Of course there are cases in which there has been compression of the nerve within the bony canal, caused by inflammation of the investing sheaths and nerve-trunk, with swelling of the parts. In these cases vision is affected; at times even to total blindness.

Now, in regard to this distension of the sheath. It is no new thing. It was noticed by some of the earlier writers, and later by Van Ammon.[2] It was shown to be due to two causes; first to direct inflammation of the sheaths themselves, by which they became very much thickened. Secondly, by a collection of fluid between the two sheaths themselves, and within the interstices of their parenchyma. In both cases the extension had a *cone-like form, the base of which was near the eye.*

If, now, this distension of the sheath is due to an inflammation of the sheath itself, either interstitial or œdematous, then we ought to find this condition of things more frequently with neuritis descendens, than in simple choked disk, and rather in the more advanced cases than in the fresh. And this is just what we do find on autopsy, as was pointed out by Graefe in his first article.[3] Here Virchow made the autopsy, and says: "The optic nerve showed in its entire length a very strongly marked thickening of the neurilemma of the nerve, and a cystoid or bladder-like separation of the same from the trunk of the nerve itself; and besides this perineuritis, there were the appearances of an interstitial neuritis for the entire length of the optic tract."

Von Ammon[4] several years before observed the same thing, and states that separation between the two sheaths to such a degree as to form bulbous projections does not, as a rule, take place before cavernous openings in the parenchyma of the sheaths themselves have been formed.

To render this more clear a cursory glance at the anatomy of the part may be of assistance.

According to the latest investigations the optic nerve is provided with an outer and inner neurilemma. The outer is called by Schwalbe, from the fact that it is a direct continuation of the dura mater, the dural sheath, the inner, from its analogy to the pia mater, the pial sheath. Between the two is a space which is called the subarachnoidal space of the optic nerve, which is the continuation of the subarachnoidal space of the brain.

---

[1] Schwalbe and Wolfring, loc. cit.

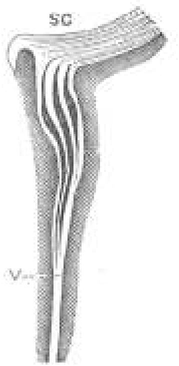
[2] Archiv für Ophth., Band vi. ab. 1. p. 15, 1860.

[3] Zehnder's Monatsblätt. 1864, p. 369. For this and other cases see, also, Archiv für Ophth., Bd. xii. ab. 2, p. 114.

[4] Archiv für Ophth., Band vi. ab. 1, p. 15, 1860.

"The dural sheath," continues Schwalbe,[1] "is the thickest of the investing membranes of the optic nerve. As this sheath is the direct continuation of the dura mater, and passes directly into the sclera, it partakes in a marked degree of the characteristics of both these membranes. Its thickness, however, is not always the same, but amounts, on the average to 0.5 m. (Henle). Towards the bulb it increases in thickness, and what was in its earlier course a single fibrous membrane, at a distance of about 7 millimetres from the entrance of the nerve into the sclera splits, at first into two or three, and finally into four lamellæ, which are separated from each other by small interspaces. Each of these divisions passes over directly into the sclera."

The drawing, which is borrowed from Schwalbe, shows this separation of the dural sheath (v) into its four lamellæ and their continuation into the sclera. (sc.) Besides the peculiar arrangement of the sheath, as shown in the drawing, there is another important anatomical point which should be kept in mind, which is, that this part is the most vascular portion of the nerve, containing, besides the vessels proper to the sheaths, ramifications from the central artery, and branches from the short ciliary arteries through the scleral ring.



Bearing this in mind, and also the fact that a neuritis, intra-ocular or otherwise, might be easily propagated to this part of the sheaths, we can readily understand why the dilatation occurs so frequently at this part of the nerve, and why it is cone-shaped with its base towards the globe. And we can further understand how it may well happen, when the inflammation has gone so far as to effect the parenchyma of the sheaths in this part, that there should be cavernous openings between the lamellæ noticed in the earlier observations.

What I wish to emphasize is that the distension of the sheath is due to disease of the sheath itself, and has no necessary connection with the fluid from the brain; and I have not seen a single case, in which the autopsy has been made by these observers, to prove that the fluid came from the brain, that the sheaths of the optic nerve were not themselves diseased, from Mitchell's case down to those reported by Dr. Norris at the last meeting of the Ophthalmological Society at Newport (1874). Again, how does it happen, as pointed out by Iwanoff[2] and von Ammon,[3] that the nerve and sheaths are sometimes found diseased at both ends, and the intermediate portions healthy?

I have, myself, seen a similar case, which was one of tumour of the

[1] Handbuch der Augenheilkunde Graefe and Sæmisch, part 1, p. 332.

[2] Zehender, 1868, p. 422.

[3] Loc. cit.

brain. The ophthalmoscopic appearances just before death were those of a virulent neuritis with much swelling of the disk and surrounding tissue. At the autopsy the sheaths of both nerves were found diseased for almost their entire length, with bulbous extensions near the globe. At about the centre of the intra-orbital portion of the nerve of the left side, there was a deep constriction of some two lines in extent; this surrounded the stem of the nerve tightly like a collar. It was caused simply by the non-extension of the nerve at this point under the inflammatory process, the sheaths being here in contact with the nerve-stem. How is it possible in such cases as these that the distension at the ocular end should be caused by fluid passing from the brain through the arachnoidal spaces, unless, indeed, it goes through the stem of the nerve and thus round the constriction? Such an explanation is certainly far-fetched, if not impossible.

These being some of the negative proofs against the theory, now for the positive.

If, in an aggregate of symptoms and appearances in any disease, we can eliminate certain existing phenomena, and the character and appearance of the disease still remain exactly the same, it is a proof positive that the excluded phenomena could not have been essential factors in the production of the disease, although they might have existed with it. So, too, if we could point to a single authenticated case made by a competent observer in which the ophthalmoscopic picture was typical of choked disk, and the autopsy showed that there was neither any disease in the nerve-trunk nor any distension of the sheaths, then it would be a proof positive that fluid from the brain could not have been the cause of the choking of the disk. Now, we can not only point to one such case, but to many. It was precisely on this point that Graefe insisted so strenuously, namely, that in those cases which were examined ophthalmoscopically by him, and at the autopsy by Virchow[1] and Schweigger,[2] the changes were limited to the *intraocular end* of the nerve—the disk—and did not extend backwards beyond the lamina cribrosa, as a rule, though in some cases the inflammation was propagated backwards towards the brain (*neuritis ascendens*.)

Is it not then more reasonable, when we find the cranial end of the nerve and its sheaths healthy, and the ocular end distended, to believe that the distension comes rather from interference with the circulation in and about the ocular end, which we know, from the labours of Zinn, Jaeger, and Leber, draws its blood from so many sources, than to believe that the fluid has filtered down through a long track without leaving a trace of its existence or passage in the nerve or its sheaths, to finally bulge out round that part of the nerve which is nearest the eye? As a single example of this, one of Iwanoff's cases may be cited. This was a case of well-marked Stauungspapille, which had been examined, for a space of three years before death, with the ophthalmoscope, by both Mauthner and Becker. It was shown by Iwanoff,[1] at the autopsy, that the changes were limited to the intraocular end of the nerve—the disk—and did not go beyond the lamina cribrosa.

---

[1] Archiv für Ophth., Band vii. ab. ii. p. 63, *et al*

[2] Ibid.

But it may be said that these examinations by Schweigger, Virchow, Iwanoff, and Von Ammon were made before Schwalbe's investigations had been made known, and that the attention of these observers was not directed critically to the condition of the sheaths. But this is precisely what it was directed towards, as they were drawing conclusions between the conditions of Stauungspapille, where only the intraocular end of the nerve was affected, and the more diffuse form of neuro-retinitis, where the nerve, not only within the cranium, but also in the orbital portion, with its sheaths, was diseased and distended.

But there are cases of autopsy made since this theory was fully ventilated, and made expressly to establish this point. For example, the case in which the autopsy was made by Mr. Swanzy, of Dublin, and figured in Allbut's book. The disease was confined to the disk, the nerve-trunk itself being perfectly normal. To this may be added the following case of Pagenstecher.[2]

The man died of a tumour in the right middle lobe as large as an orange, which the examination showed to consist of a large, irregular mass, like clotted blood in various stages of transformation. Before death there were the ophthalmoscopic appearances of choked disk. At the autopsy the size, colour, and consistence of both nerves appeared perfectly normal throughout their entire course up to the globe.

"The exterior and interior sheath, as well as the intervening connective tissue, do not exhibit any abnormality even in the immediate neighbourhood of the bulb. The changes were limited to the lamina cribrosa." And what is more, the autopsy showed that not only was there no fluid between the sheaths, but also that there was none in the cranial cavity, for "the cranial bones were remarkably thin and diaphanous. The dura mater was natural. The proper membranes dry on surface from swelling of the brain. No lymph anywhere."

I have myself seen two cases where there were all the ophthalmoscopic signs of choked disk during life, and where the autopsy showed a reduction of the normal quantity of fluid in the cranial cavity.

Again, how can we explain the occurrence of Stauungspapille in a single eye on this principle? For, if the fluid was forced through one optic foramen, why should it not be through the other? It may be suggested that the growth might occupy such a position as to shut off the

[1] Zehender, 1868, p. 442.

[2] Ophth. Hospital Reports, vol. vii., pt. 2, p. 126.

fluid from the optic foramen of one side, and allow it to pass to the other. But this cannot hold good, as is conclusively proved by some cases, of which the following, from Pagenstecher, is an example.[1]

> "The patient died from a large gliomatous tumour in the left hemisphere. The left eye, at the autopsy, was seen to be perfectly normal, while in the right the papilla was very prominent, measuring four times the height of the left from the lamina cribrosa. There was an enormous distension of the external sheath *near the eye*, but at about the distance of half an inch from the insertion of the nerve into the sclera this pretty closely invested the nerve, while in the other eye the sheaths bore their normal relations to the trunk of the nerve."

Such cases of one-sided neuritis are utterly irreconcilable with the theory that the choking of the disk has been caused by fluid being forced from the brain between the two sheaths of the optic nerve. They are also inconsistent with Graefe's theory of a general increase of pressure which is equally distributed through the cranial cavity. They could only exist under the pressure theory with the admission that the pressure, instead of being equally distributed through the whole brain, might be restricted to a particular region. That such a restriction might exist does not from anatomical reasons appear impossible or indeed improbable. This would apply especially to the base of the brain, or to that portion which lies beneath the tentorium.

It would seem then, if the foregoing arguments are of any value, that, although Graefe's division of neuritis into two kinds—the descending and ascending—is borne out, his explanation of the cause of choked disk is insufficient, though it must be admitted that increased intra-cranial pressure is an important factor in its production.

It would also appear that the theory of the production of choked disk based on fluid passing from the cranial cavity between the two sheaths of the nerve is untenable; and further, that the appearance of the fluid at the ocular end of the nerve is rather the result of a diseased condition of the trunk and sheaths of the nerve than a cause of choked disk.

It would seem then, after all, that Benedikt's theory is the least assailable, though it may be so, as some claim, because it is the least demonstrable.

In view of these facts, might not the true explanation be found in a combination of the two theories?—that is, that choked disk, in connection with brain disease, is the expression of a compression within the head of certain nerves, and that the effect is transmitted along such nerve fibres as run to the eye and preside over the blood supply and maintain the healthy processes of waste and repair at the disk, on precisely analogous grounds as that the cornea is affected in certain morbid conditions of the fifth pair.

---

[1] Ophth. Hospital Reports, vol. vii.

This interference with the normal condition of the nerves by compression might then take place from various causes, either by imprisonment of the fibres by the morbid growth, or by direct pressure by this latter upon the nerves. Again, it might occur by a general elevation of the intra-cranial pressure, which extended equally in all directions, or which was confined to a particular region. The fact that the cavernous sinus contains branches of the sympathetic system might have some weight in the question.

My excuse for dwelling so long on so technical a point is so much better expressed in the words of a colleague, that I most willingly shield myself behind them. Dr. Noyes, in his recent report on ophthalmic literature, says :—

> "The researches of Schwalbe and Schmidt have done so much to establish an intimate connection between the optic papilla and the brain, both in anatomy and pathology, that the subject cannot be dropped until it has been completely exhausted. In fact, it is imperative that we should possess the most absolute and complete knowledge of the whole matter. Without it our inferences from the phenomena of the optic disk must be uncertain and vague. On the one hand, we should fail to properly appreciate all that occurs in intraocular pathology, and still more egregiously must we miss the mark when we begin to reason from these data to intra-cranial lesions. The papers above quoted supply us with important facts. But, with the most exact knowledge we can have, can any critical and logical observer with the ophthalmoscope be willing to use the word cerebroscopy when he is studying only the optic papilla?"

This question, so far as our present knowledge extends, must certainly be answered in the negative, for the simple reason that it is becoming every day more apparent that we may have the ophthalmoscopic appearances which are typical of choked disk, and which are not connected with any cerebral trouble whatever, but are due simply to some orbital or even intraocular disease.

Interesting and important as the investigations of Hiss, Arnold, Schwalbe, and others into the lymph spaces of the brain and eye really are, they nevertheless do not appear to have cast any light upon the etiology of choked disk, the true cause of which seems to be as great a mystery as ever.

It is unnecessary for me to add a single word in regard to the great merits of the ophthalmoscope as an essential, at times even an indispensable, agent in the diagnosis of brain disease. This is recognized throughout the world. It is only the ignorant who alike underrate its virtues or over-estimate its capabilities.